

WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

A1

(51) International Patent Classification ⁶:

C07D 215/54, A61K 31/47, C07D 241/44,
A61K 31/50, C07D 213/82, A61K 31/455,
C07D 217/26, 237/28, A61K 31/495,
C07D 307/85, A61K 31/34, C07D 333/70,
A61K 31/38, C07D 235/24, A61K 31/415,
C07D 241/24, 209/42, A61K 31/40, C07D
277/68, A61K 31/425, C07D 221/04,
213/81, 405/12, 401/12, 409/12, 417/12,
403/12, 471/04 // (C07D 471/04, 231:00,
221:00)

(11) International Publication Number:

WO 98/38167

(43) International Publication Date:

3 September 1998 (03.09.98)

(21) International Application Number:

PCT/US98/01568

(22) International Filing Date:

5 February 1998 (05.02.98)

(30) Priority Data:

60/039.169

26 February 1997 (26.02.97) US

(71) Applicant (for all designated States except US): PFIZER INC. [US/US]; 235 East 42nd Street, New York, NY 10017 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): BROWN, Matthew, Frank [US/US]; 66 Greenhaven Road, Pawcatuck, CT 06379 (US). KATH, John, Charles [US/US]; 252 Shore Road, Waterford, CT 06385 (US). POSS, Christopher, Stanley [US/US]; 10 Hermitage Drive, Gales Ferry, CT 06335 (US).

(74) Agents: SPIEGEL, Allen, J. et al.; Pfizer Inc., Patent Dept., 235 East 42nd Street, New York, NY 10017 (US).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published

With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: HETEROARYL-HEXANOIC ACID AMIDE DERIVATIVES, THEIR PREPARATION AND THEIR USE AS SELECTIVE INHIBITORS OF MIP-1-ALPHA BINDING TO ITS CCR1 RECEPTOR

(57) Abstract

 $\begin{array}{c|cccc} Compounds & of & formula \\ (I) & wherein & R^1 & is & optionally \\ substituted & (C_2-C_9)heteroaryl; \\ R^2 & is & optionally & substituted & phenyl-(CH_2)_m-, \\ naphthyl-(CH_2)_m-, \end{array}$

 (C_3-C_{10}) cycloalkyl- $(CH_2)_m$ -, (C_1-C_6) alkyl or (C_2-C_9) heteroaryl- $(CH_2)_m$ -, m is an integer from zero to four; R^3 is hydrogen, or optionally substituted (C_1-C_{10}) alkyl, (C_3-C_{10}) cycloalkyl- $(CH_2)_m$ -, (C_2-C_9) heterocycloalkyl- $(CH_2)_m$ -, (C_2-C_9) heteroaryl- $(CH_2)_m$ - or aryl- $(CH_2)_m$ -, n is an integer from zero to six; or R^3 and the carbon to which it is attached form an optionally substituted and/or fused five to seven membered carbocyclic ring; R^4 substituted (C_1-C_6) alkyl, hydroxy, (C_1-C_6) alkoxy, hydroxy (C_1-C_6) alkoxy, hydroxy, (C_1-C_6) alkoxy, hydroxy, (C_1-C_6) alkoxy, hydroxy, (C_1-C_6) alkoxy, hydroxy, (C_1-C_6) alkoxy, hydroxy, or optionally substituted (C_2-C_9) heterocycloalkyl- $(CH_2)_p$ -, or optionally substituted (C_2-C_9) heterocycloalkyl group; R^5 is hydrogen, (C_1-C_6) alkyl or amino. The present compounds are potent and selective inhibitors of MIP-1-alpha. binding to its receptor CCR1, and are thus useful to treat inflammation and other immune disorders.